REMARKS

Reconsideration of this application is respectfully requested in view of the foregoing amendments and the following remarks. Claims 1-24 and 26-32 were pending in this Application. Claim 27 has been amended, and claims 21-24 remain withdrawn. Accordingly claims 1-20 and 26-32 are presently under examination. Support for the amendments may be found, for example, in the original claims, and in the specification at page 7 lines 26-28. No new matter has been introduced.

In the Office Action:

- Claims 1-19 and 26-31 were rejected under 35 U.S.C. §103(a) as obvious over Struengmann et al. (U.S. Patent No. 6,284,269; hereinafter "Struengmann") in view of Bock et al. (U.S. Patent No. 6,869,948; hereinafter "Bock") and Robinson et al. (U.S. Patent No. 6,071,539; hereinafter "Robinson").
- Claims 20 and 32 were rejected under 35 U.S.C. §103(a) as obvious over Struengmann in view of Bock and Ouali.

Applicants respectfully traverse the rejections and submit that all claims pending herein are in condition for immediate allowance, for the reasons set forth below.

A. The Claimed Invention and its "Basic and Novel Characteristics"

Claims 1 and 27 recite ***water soluble granules*** comprising meloxicam and a salt forming agent, wherein 5 g of said granules ***dissolve*** in 100mL of demineralized water ***in about 1 minute*** to form a clear solution. This limitation regarding the speed of dissolution of the granules is not taught or suggested by any of the cited prior art references. Accordingly, claims 1 and 27 and all their dependents are in condition for immediate allowance.

Claims 20 and 32 recite water soluble granules comprising (claim 20) or consisting essentially of (claim 32) meloxicam, meglumine, hydroxypropylmethylcellulose, soluble povidone, and glucose monohydrate. None of the cited prior art references teach or suggest such a composition. Accordingly, claims 20 and 32 are in condition for immediate allowance.

With respect to claims 27-30 and 32, the Office argued that Applicants have failed to define what compounds materially affect the basic and novel characteristics of the claimed invention. Office Action at pages 6 and 8. Applicants respectfully disagree.

The situation here is highly analogous to the exemplary *AK Steel Corp.* case cited in MPEP § 2111.03. In *AK Steel*, the patent claimed a "coating metal consisting essentially of aluminum." *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1237 (Fed. Cir. 2003). The Federal Circuit examined the specification of the patent, which "states that good wetting is the goal of the invention" and also states that "'silicon contents in the coating metal should not exceed about 0.5% by weight'". In view of these statements in the specification, the Federal Circuit held that "silicon in excess of 0.5% by weight would materially alter the basic and novel properties of the invention." *Id.* at 1240.

Like the patent in *AK Steel*, ***the present Application states a goal: water soluble granules containing meloxicam***. For example, the present Application is entitled "Water-Soluble Meloxicam Granules" and discloses that:

- "meloxicam...does not dissolve readily in water" (page 1 lines 19-20);
- "The aim of the present invention is therefore to develop a granulated form of meloxicam which can be administered to the animals by mixing it into their drinking water" (page 1 line 30 through page 2 line 1);
- "The invention therefore relates to water soluble meloxicam granules..." (page 2 line 10);
- "The meloxicam granules according to the invention have a number of advantages over existing preparations. ... Because of the good solubility of the meloxicam granules according to the invention in water..." (page 2 lines 15-21); and
- "The total solubility of the granules in water ensures optical control of a totally dissolved active substance..." (page 2 lines 26-27).

Further, 22 of the original 24 claims specifically recited the term "water soluble" in the claims.

Just as the Federal Circuit in *AK Steel* was able to determine what "materially affects the basic and novel properties of the invention" by "look[ing] no further than the specification", the person skilled in the art here would understand that the goal of the present Application is to

achieve water solubility of meloxicam granules, and thus that the "basic and novel characteristics" of the claimed invention are ***water-soluble*** granules of meloxicam.

Accordingly, for the claims that recite water soluble particles "consisting essentially of" meloxicam and other components (claims 27-32), the person skilled in the art would understand that the addition of insoluble components that would, by composition or amount, affect this basic and novel water-solubility of the claimed granules is excluded by the use of the term "consisting essentially" in the claims.

B. The Rejection of Claims 1-19 and 26-31

The Office contends that Struengmann teaches "fast disintegrating meloxicam formulations", that Bock discloses granular formulations of meloxicam salts, that Ouali teaches various fillers, and that Robinson teaches granules containing sweeteners and flavors. Applicants respectfully disagree with the Office that Struengmann, either alone or in combination with the secondary references, teaches or suggests the claimed granules or methods, because the cited art fails to teach or suggest water soluble granules, or indeed any granules containing meloxicam salts.

With respect to Struengmann, the Office argues that Example V/9 teaches a tablet that is fast-dissolving and that contains 1.8% meloxicam, 87% carrier, 2.4% sweetener and 1.2% binder. Office Action at pages 3-4. The Office admits that Struengmann fails to teach a meglumine salt of meloxicam, and also fails to teach the claimed flavorants (e.g., vanilla, honey, etc.). The Office argues that Bock teaches a granular formulation of meloxicam having a high amount of carrier and comprising a meloxicam salt, that Robinson teaches effervescent granules, and that Ouali teaches HPMC and other excipients. Office Action at pages 4-5. Applicants respectfully disagree that such disclosures, whether alone or in combination, teach or suggest the claimed invention.

Independent claims 1 and 27 require that the granules are water soluble, and that 5 g of the granules dissolve in 100mL of demineralized water in about 1 minute to form a clear solution. Struengmann fails to teach or suggest the claimed granules either alone or in combination with the secondary references. Example V/9 of Struengmann discloses a tablet containing 7.5 mg meloxicam (not the 58 mg asserted by the Office). The meloxicam is present

as a "meloxicam composition according to example IV/1". Struengmann at col. 11 lines 43-56. Turning to Example IV/1, a powder composition is formed from 11.35 g beta-cyclodextrin and 1.76 g meloxicam (total weight 13.01 g), and its "in vitro rates of dissolution" are disclosed in Table 4 at col. 5 lines 20-35 of Struengmann. It is apparent from Table 4 that ***partial dissolution*** of the powder composition of example IV/1 occurs over a period of time of up to 60 minutes, and thus that the powder composition cannot satisfy the claimed ***formation of a clear solution in about 1 minute***. No dissolution information is provided for the tablet composition of Example V/9, which contains only 58 mg of the composition of Example IV/1 (and thus only 7.5 mg meloxicam). Thus, nothing in Struengmann indicates "fast" disintegration as the Office asserts, nor that its compositions could be capable of the claimed formation of a clear solution in about 1 minute.

The secondary references fail to supplement these defects. The granules of Bock require about an hour to achieve ***release*** of meloxicam, see Bock at FIG. 3, however nothing is mentioned about whether such "release" is in any way equivalent to the claimed formation of a solution. Further, the particles of Bock contain a ***high amount of insoluble material, and therefore are not water soluble***. The granules of Bock in Examples 6 and 7 contain over 51% (Example 6) and 67% (Example 7) insoluble ingredients (not even counting the additional 1.7 to 4.2% insoluble meloxicam), such as cross-linked polyvinylpyrrolidone, microcrystalline cellulose and silicon dioxide. Thus, ***it is not chemically possible for such granules to be water soluble***. *See, e.g.*, Declaration of Dr. Martin Folger submitted on May 11, 2009, at paragraphs 15, 20. Nor do Struengmann or Bock's compositions comprise a salt of meloxicam (the meloxicam salts disclosed in Example 1 and 7 of Bock are not in granular form).

Struengmann and Bock thus fail to teach or suggest water soluble granules comprising meloxicam salts, or such granules wherein 5 g of the granules dissolve in 100mL of demineralized water in about 1 minute to form a clear solution. The secondary references fail to supplement these deficiencies. Neither Ouali nor Robinson teach or suggest water soluble granules of any type, meloxicam salts in granular form, or meloxicam granules wherein 5 g of the granules dissolve in 100mL of demineralized water in about 1 minute to form a clear solution. Thus, even the combination of Ouali and Robinson with both Struengmann and Bock fails to teach or suggest the present independent claims.

In addition, a *prima facie* case of obviousness has not been established because the Office has not provided any support for the conclusion that there existed at the time of the invention an apparent reason to modify the tablet of Struengmann or the insoluble granules of Bock to alter their solubility, components, or form (e.g., use a meloxicam salt). "[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *See KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740-41, 82 USPQ2d 1385, 1396 (2007); *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). *See also* MPEP § 2141. The Office's cited rationale that a person of ordinary skill in the art would combine the cited references in the manner suggested is just such a conclusory statement. For example, the mere fact that meloxicam salts exist does not establish that a person skilled in the art would consider them advantageous in a particular application, and the advantages of using salts or changing the components of a formulation are hardly the type of fact that is of such "instant and unquestionable demonstration" that would permit Official Notice to be taken unsupported by any evidence, such as the Examiner has done here. See MPEP § 2144.03 ("Official notice unsupported by documentary evidence should only be taken by the examiner where the facts ... are capable of instant and unquestionable demonstration").

As explained above, ***none of the cited references teaches water soluble granules of any type***, let alone water soluble granules containing meloxicam salts wherein 5 g of the granules dissolve in 100mL of demineralized water in about 1 minute to form a clear solution. As evident from the discussed disclosures of Struengmann and Bock, the person skilled in the art would need to change almost all or all components of the prior art particles in order to achieve the claimed invention. Such radical alterations are not within the realm of obvious substitutions as the Office asserts.

The Office claims that it is merely "ordinary skill" to turn the tablet of Struengmann or the insoluble granules of Bock into soluble granules having the claimed ability to form a solution in about 1 minute, but provides no rational underpinning for this bold statement that goes far beyond what any of the cited references teaches or even suggests. The skilled artisan would not have expected that the tablet of Struengmann or the insoluble granules of Bock could be modified in the absence of any guidance in the art to result in a water soluble granule

containing meloxicam salts wherein 5 g of the granules dissolve in 100mL of demineralized water in about 1 minute to form a clear solution, let alone with any degree of predictability.

Without using Applicants' claimed invention as a roadmap, ***there is no guidance for the artisan to modify Struengmann or Bock.*** It is well-established law that obviousness cannot be proven using hindsight, that is, it "is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious." *In re Fritch*, 23 U.S.P.Q.2d 1780, 1784 (Fed. Cir. 1992). *See also In re Gorman*, 933 F.2d 982, 987 (Fed. Cir. 1991) ("It is impermissible ... simply to engage in a hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps."). This law has not been obviated by the Supreme Court's *KSR* decision. As explained in the post-*KSR* case of *Takeda Chemical Indus. v. Alphapharm Pty.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007), it "remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound." No such reason is found here.

C. The Rejection of Claims 20 and 32

Independent claims 20 and 32 require that the granules are water soluble, and comprise or consist essentially of meloxicam, meglumine, hydroxypropylmethylcellulose, soluble povidone, and glucose monohydrate. Struengmann fails to teach or suggest the claimed granules either alone or in combination with the secondary references.

Example V/9 of Struengmann discloses a tablet that contains meloxicam, but no granules, and none of the other claimed components. Applicants note that polyvinylpyrrolidone (povidone) occurs in both soluble and insoluble forms, and Struengmann does not specify which is present in its composition. Because the tablet of Struengmann contains insoluble components, such as polydimethylsiloxane, nothing in Struengmann teaches or suggests that the polyvinylpyrrolidone is soluble.

Bock likewise fails to disclose the compositions of claims 20 and 32. At Example 6 Bock discloses a tablet containing meloxicam, but none of the other claimed components, and at

Example 7 Bock discloses a capsule containing meloxicam and soluble povidone, but no other claimed components. Ouali teaches enterically-coated NSAID and prostaglandin compositions containing stabilizing agents. Ouali fails to disclose the compositions of claims 20 and 32, or indeed any composition comprising meloxicam or the other claimed components.

The Office argues that Ouali teaches a list of binders including glucose, polyvinylpyrrolidone and HPMC, and that "as it is known that glucose and HPMC are known binders, it would be obvious to employ them in the granule of Struengmann and Bock." Office Action at pages 6-7.

Applicants respectfully disagree that the cited art teaches or suggests the claimed granules. None of the cited art references teach or suggest water-soluble granules comprising meloxicam, let alone in conjunction with the other claimed components. Merely because the Office asserts that a component such as glucose is known to exist does not make its combination with meloxicam and the other claimed components obvious, and such conclusory arguments cannot support a *prima facie* case of obviousness. The Office has not provided any support for the conclusion that there existed at the time of the invention an apparent reason to modify the tablet of Struengmann or the insoluble granules of Bock to alter their solubility, components, or form (e.g., use a meloxicam salt). "[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *See KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740-41, 82 USPQ2d 1385, 1396 (2007); *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). *See also* MPEP § 2141.

The Office's cited rationale that a person of ordinary skill in the art would combine the cited references in the manner suggested is just such a conclusory statement. For example, the mere fact that meloxicam salts exist does not establish that a person skilled in the art would consider them advantageous in a particular application, and the advantages of using salts or changing the components of a formulation are hardly the type of fact that is of such "instant and unquestionable demonstration" that would permit Official Notice to be taken unsupported by any evidence, such as the Examiner has done here. See MPEP § 2144.03 ("Official notice unsupported by documentary evidence should only be taken by the examiner where the facts … are capable of instant and unquestionable demonstration").

As explained above, ***none of the cited references teaches water soluble granules of any type***, let alone water soluble granules containing meloxicam, meglumine, hydroxypropylmethylcellulose, soluble povidone, and glucose monohydrate. As evident from the discussed disclosures of Struengmann and Bock, the person skilled in the art would need to change almost all or all components of the prior art particles in order to achieve the claimed invention. Such radical alterations are not within the realm of obvious substitutions as the Office asserts.

The Office claims that it is merely "ordinary skill" to turn the tablet of Struengmann or the insoluble granules of Bock into soluble granules containing the precise claimed compositions, but provides no rational underpinning for this bold statement that goes far beyond what any of the cited references teaches or even suggests. Without using Applicants' claimed invention as a roadmap, ***there is no guidance for the artisan to modify Struengmann or Bock.*** It is well-established law that obviousness cannot be proven using hindsight, that is, it "is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious." *In re Fritch*, 23 U.S.P.Q.2d 1780, 1784 (Fed. Cir. 1992). *See also In re Gorman*, 933 F.2d 982, 987 (Fed. Cir. 1991) ("It is impermissible ... simply to engage in a hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps."). This law has not been obviated by the Supreme Court's *KSR* decision. As explained in the post-*KSR* case of *Takeda Chemical Indus. v. Alphapharm Pty.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007), it "remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound." No such reason is found here.

In conclusion, the cited references taken alone or in combination do not teach, suggest, or make obvious the present invention, and Applicants respectfully request that the rejections be withdrawn. In view of the foregoing, all of the claims in this case are believed to be in condition for allowance. Should the Examiner have any questions or determine that any further action is desirable to place this application in even better condition for issue, the Examiner is encouraged to telephone Applicants' undersigned representative.

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